CLAIMS

What is claimed is:

1. A method for identifying an agent that modulates sphingolipid metabolism, comprising:

(a) culturing a mutant yeast strain with sphingosine in the absence and presence of a candidate agent under conditions and for a time sufficient to observe in said mutant yeast strain an altered level of either (i) at least one sphingolipid intermediate, or (ii) activity of at least one component of a sphingolipid pathway, wherein:

the mutant yeast strain comprises a null allele of at least one gene encoding a component of a sphingolipid pathway that results in an altered activity level of at least one sphingolipid pathway component, and wherein said mutant strain of yeast has been genetically altered to express at least one nonendogenous sphingolipid pathway component and wherein the mutant yeast strain exhibits growth inhibition in the presence of sphingosine; and

(b) comparing growth of the mutant yeast strain in the presence of the candidate agent to the growth of the mutant yeast strain in the absence of the candidate agent, wherein an increase in growth of the mutant yeast strain in the presence of the agent indicates the agent modulates sphingolipid metabolism.

2. The method of claim 1 wherein said at least one gene comprises DPL1.

3. The method of claim 1 wherein said at least one gene comprises DPL1 and LCB4.

4. The method of claim 3 wherein said at least one nonendogenous sphingolipid pathway component comprises human SPHK1.

5. The method of claim 4 wherein the altered level of the sphingolipid intermediate in the presence of the candidate agent comprises a decrease in at least one LCBP.

6. The method of claim 5 wherein said at least one LCBP comprises sphingosine-1-phosphate.

7. The method of claim 4 wherein the altered level of the activity of the sphingolipid pathway component in the presence of the candidate agent comprises a decrease in the human SPHK1 activity.

8. A method for identifying an inhibitor of SK, comprising:

(a) culturing a null mutant yeast strain with sphingosine in the absence and presence of a candidate agent under conditions and for a time sufficient to observe in said mutant yeast strain an altered ability of said yeast mutant strain to grow, wherein:

the mutant yeast strain comprises a null allele of at least DPL1 and LCB4, and wherein said mutant strain of yeast has been genetically altered to express nonendogenous SK and wherein the mutant yeast strain exhibits growth inhibition in the presence of sphingosine; and

(b) comparing growth of the mutant yeast strain in the presence of the candidate agent to the growth of the mutant yeast strain in the absence of the candidate agent, wherein an increase in growth of said mutant yeast strain in the presence of the agent indicates the agent is an inhibitor of SK.

9. A method for identifying an inhibitor of SK, comprising:

(a) culturing a null mutant yeast strain with an inducer in the absence and presence of a candidate agent under conditions and for a time sufficient to observe altered growth in said mutant yeast strain, wherein:

the mutant yeast strain comprises a null allele of at least DPL1, LCB4, and SPP, and wherein said mutant strain of yeast has been genetically altered to express nonendogenous SK under the control of a promoter that is induced by the inducer and wherein the mutant yeast strain exhibits growth inhibition in the presence of the inducer; and

(b) comparing growth of the mutant yeast strain in the presence of the candidate agent to the growth of the mutant yeast strain in the absence of the candidate agent, wherein an increase in growth of said mutant yeast strain in the presence of the candidate agent indicates the candidate agent is an inhibitor of SK.

10. The method of claim 9 wherein said inducible promoter is a galactose-inducible promoter.

11. The method of claim 10 wherein said inducer is galactose.

12. A method for identifying an agent that modulates sphingolipid metabolism, comprising:

(a) culturing a mutant yeast strain with sphingosine in the absence and presence of a candidate agent under conditions and for a time sufficient to observe in said mutant yeast strain an altered level of either (i) at least one sphingolipid intermediate, or (ii) activity of at least one component of a sphingolipid pathway, wherein:

the mutant yeast strain comprises a null allele of at least one gene encoding a component of a sphingolipid pathway that results in an altered activity level of at least one sphingolipid pathway component, and wherein said mutant strain of yeast has been genetically altered to express at least one nonendogenous sphingolipid

pathway component and wherein the mutant yeast strain exhibits growth inhibition in the presence of sphingosine; and

(b) comparing the level of either (i) or (ii) in the mutant yeast strain cultured in the presence of the candidate agent to the level of either (i) or (ii) in the mutant yeast strain cultured in the absence of the candidate agent, wherein an altered level in the presence of the agent indicates the agent modulates sphingolipid metabolism.

13. The method of claim 12 wherein said altered level of said at least one sphingolipid intermediate comprises a decrease in S-1-P.

14. The method of claim 13 wherein said altered level of said activity of at least one component of a sphingolipid pathway comprises a decrease in the activity of said at least one nonendogenous sphingolipid pathway component.

15. The method of claim 14 wherein said at least one nonendogenous sphingolipid pathway component comprises human SPHK1.

16. A method for identifying an agent that modulates sphingolipid metabolism, comprising:

(a) culturing a null mutant yeast strain with sphingosine in the absence and presence of a candidate agent under conditions and for a time sufficient to observe altered growth of said mutant yeast strain, wherein:

the mutant yeast strain comprises a null allele of at least one gene encoding a component of a sphingolipid pathway that results in an altered activity level of at least one sphingolipid pathway component, and wherein said mutant strain of yeast has been genetically altered to express at least one nonendogenous sphingolipid pathway component, and wherein the mutant yeast strain exhibits growth inhibition in the presence of sphingosine; and

(b) comparing growth of the mutant yeast strain in the presence of the candidate agent to growth of the mutant yeast strain in the absence of the candidate agent, wherein an increase in growth of said mutant yeast strain in the presence of the candidate agent indicates the agent modulates sphingolipid metabolism.

17. The method of claim 16 wherein said at least one gene comprises DPL1.

18. The method of claim 16 wherein said at least one gene comprises DPL1 and LCB4.

19. The method of claim 16 wherein said at least one nonendogenous sphingolipid pathway component comprises human SPHK1.

20. A method for identifying an agent that modulates sphingolipid metabolism, comprising:

(a) culturing a mutant yeast strain with an inducer in the absence and presence of a candidate agent under conditions and for a time sufficient to observe in said mutant yeast strain an altered level of either (i) at least one sphingolipid intermediate, or (ii) activity of at least one component of a sphingolipid pathway, wherein:

the mutant yeast strain comprises a null allele of at least one gene encoding a component of a sphingolipid pathway that results in an altered activity level of at least one sphingolipid pathway component, and wherein said mutant strain of yeast has been genetically altered to express at least one nonendogenous sphingolipid pathway component under the control of a promoter that is induced by the inducer and wherein the mutant yeast strain exhibits growth inhibition in the presence of the inducer; and

(b) comparing the level of either (i) or (ii) in the mutant yeast strain cultured in the presence of the candidate agent to the level of either (i) or (ii) in the mutant yeast strain cultured in the absence of the candidate agent, wherein an altered level in the presence of the agent indicates the agent modulates sphingolipid metabolism.

21. The method of claim 20 wherein said altered level of said at least one sphingolipid intermediate comprises a decrease in LCBPs.

22. The method of claim 20 wherein said altered level of said activity of at least one component of a sphingolipid pathway comprises a decrease in the activity of said at least one nonendogenous sphingolipid pathway component.

23. The method of claim 22 wherein said at least one nonendogenous sphingolipid pathway component comprises human SPHK1.

24. The method of claim 20 wherein said at least one gene comprises DPL1.

25. The method of claim 20 wherein said at least one gene comprises DPL1 and LCB4.

26. The method of claim 20 wherein said at least one gene comprises DPL1, LCB4, and YSR2.

27. A method for identifying an agent that modulates sphingolipid metabolism, comprising:

(a) culturing a null mutant yeast strain with an inducer in the absence and presence of a candidate agent under conditions and for a time sufficient to observe altered growth of said mutant yeast strain, wherein:

the mutant yeast strain comprises a null allele of at least one gene encoding a component of a sphingolipid pathway that results in an altered activity level of at least one sphingolipid pathway component, and wherein said mutant strain of yeast has been genetically altered to express at least one nonendogenous sphingolipid pathway component under the control of a promoter that is induced by the inducer and wherein the mutant yeast strain exhibits growth inhibition in the presence of the inducer; and

(b) comparing growth of the mutant yeast strain in the presence of the candidate agent to growth of the mutant yeast strain in the absence of the candidate agent, wherein an increase in growth of said mutant yeast strain in the presence of the candidate agent indicates the agent modulates sphingolipid metabolism.

28. The method of claim 27 wherein said at least one gene comprises DPL1.

29. The method of claim 27 wherein said at least one gene comprises DPL1 and LCB4.

30. The method of claim 27 wherein said at least one gene comprises DPL1, LCB4, and YSR2.

31. The method of claim 30 wherein said at least one nonendogenous sphingolipid pathway component comprises human SPHK1.